DETAILED ACTION

Claims 1-8, 10 as amended and new claims 15-21 (1/04/2010) are under examination in the instant office action.

This application contains claims 11-14 drawn to an invention nonelected with traverse in the reply filed on 4/10/2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 as amended is rendered indefinite by the phrase "cell containing a liquid nutritive base". The meaning of this phrase is unclear.

Claim 4 as amended is now lacking poloxamer. Thus, it is unclear for what ingredients that claimed amounts are intended.

Claims 17 and 18 recite the limitation "cellulose" in the medium with methylcellulose of claim 6. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5-8, 10 as amended and new claims 17-21 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/32929 (IDS reference).

Claims are directed to a preservation medium for living organs, biological tissues, and cells wherein the medium comprises a high-molecular-weight hyaluronic acid, sodium chloride, trace elements, amino acids, vitamins and stabilizing pH buffer; and wherein the medium is free from components of animal origin. Some claims are further drawn to the amounts of hyaluronic acids 80-4,000 mg/L or 100-200 mg/L or 100-160 mg/L, to the amounts of sodium chloride 4,500-9,000mg/L or 5,500-9,000mg/L or 7,000 mg/L of sodium chloride in the medium. Some claims are further drawn to incorporation methyl cellulose in the medium in amounts 210-5,000 mg/L or 1,900-2,500 mg/L or 2,205 mg/L. Some claims are further drawn to the medium osmolarity being from 300- 465 mOsm +/- 40 mOsm. Some claims are further drawn to the medium Brookfield viscosity at 20 °C in the range between 1-15 centipoises or 2.5-10 centipoises. Some claims are further drawn to the exclusion of dextran.

WO 96/32929 discloses an ophthalmic solution or a preservation medium for living organs, biological tissues and cells wherein the medium comprises a liquid nutritive base, a high-molecular-weight HA and sodium chloride and wherein the medium is free from components of animal origin (entire document). The cited medium contains HA in amounts 0.1-5 % (page 5, last par. or page 7, par. 3), sodium chloride in amounts 0.01-1% (page 7). The medium osmolarity is in the range 200-600 mOsm (page 7). The cited document also teaches incorporation of methyl cellulose (page 14, line 4-5) in the medium in amounts 0.1-5% (page 14, lines 4-6). The medium also contains salts or trace elements, pH buffer stabilizer or buffering agents and glutathione that contain aminoacids and that is a generic vitamin. The dextran is absent. The cited medium

contains same components in the same amounts as required for the claimed medium and, therefore, it is reasonably expected to present identical viscosity as intended for the claimed medium. Thus, the cited document WO 96/32929 anticipates the claimed invention.

Claims 1-4, 7, 8, 10 as amended and new claims 16, 19-21 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,102,783 (Alkemade et al).

Claims are directed to a preservation medium for living organs, biological tissues, and cells wherein the medium comprises a high-molecular-weight hyaluronic acid, sodium chloride, trace elements, amino acids, vitamins and stabilizing pH buffer; and wherein the medium is free from components of animal origin. Some claims are further drawn to the amounts of hyaluronic acids 80-4,000 mg/L or 100-200 mg/L or 100-160 mg/L, to the amounts of sodium chloride 4,500-9,000mg/L or 5,500-9,000mg/L or 7,000 mg/L of sodium chloride in the medium. Some claims are further drawn to incorporation of 200-75,000 mg/L or 450- 50,000 mg/L of poloxamer 188 in the medium. Some claims are further drawn to the medium osmolarity being from 300-465 mOsm +/- 40 mOsm. Some claims are further drawn to the medium Brookfield viscosity at 20°C in the range between 1-15 centipoises or 2.5-10 centipoises. Some claims are further drawn to the exclusion of dextran.

US 5,102,783 (Alkemade et al) (same disclosure as in the IDS reference WO 92/21234) teaches a preservation medium for living organs, biological tissues and cells (entire document), wherein the medium comprises high-molecular-weight HA in amounts 10 mg/L – 10,000 mg/L (col. 5, lines 60-68) including sodium hyaluronate form when dissolved in balanced salt solution (table at col. 6). The cited document teaches incorporation of a liquid nutritive base that is a

conventional medium Ham's F-10, for example: col. 4, line 23. The medium Ham's 10 contains sodium chloride in amounts about 0.7% or 7400 mg/L (ATCC catalogue page 518). The conventional media including Ham's F-10 that is incorporated into the final preservation medium also contains trace elements, amino acids, pH buffering agents within the meaning of the claims. The osmolarity of cited medium that is based on ingredients and amounts of conventional cell culture media and it would fall within the physiologically acceptable ranges as claimed (col. 4, lines 30-35). The cited document teaches that HA provides for viscosity in the medium (col. 5, lines 28-38) and, thus, it would be reasonably to expect that the viscosity of the cited medium is the same as claimed because the cited document teaches the use of the same HA amounts as required for the claimed invention. US 5,102,783 further teaches incorporation of poloxamer 188 in amounts from 0.05 mg/ml or 50 mg/L to 10 mg/ml or 10,000 mg/L (col. 6, lines 23-29). The dextran is absent. US 5,102,783 explicitly teaches substitution of HA for serum that is a component of animal origin for the benefit in reducing potential microbial and viral contamination.

The cited medium contains same components in the same amounts as required for the claimed medium and, therefore, it is reasonably expected to present identical viscosity as intended for the claimed medium.

Thus, the cited document US 5,102,783 anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 10 as amended and new claims 16-21 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over DERWENT publication XP 002036193 of JP 6107538 (IDS reference), WO 96/32929 (IDS reference) and US 5,102,783 (Alkemade et al).

Claims are directed to a preservation medium for living organs, biological tissues, and cells wherein the medium comprises a high-molecular-weight hyaluronic acid, sodium chloride, trace elements, amino acids, vitamins and stabilizing pH buffer; and wherein the medium is free from components of animal origin.

Some claims are further drawn to the amounts of hyaluronic acids 80-4,000 mg/L or 100-200 mg/L or 100-160 mg/L, to the amounts of sodium chloride 4,500-9,000mg/L or 5,500-9,000mg/L or 7,000 mg/L of sodium chloride in the medium. Some claims are further drawn to incorporation of 200-75,000 mg/L or 450- 50,000 mg/L of poloxamer 188 in the medium. Some claims are further drawn to incorporation methyl cellulose in the medium in amounts 210-5,000 mg/L or 1,900-2,500 mg/L or 2,205 mg/L. Some claims are further drawn to the medium osmolarity being from 300- 465 mOsm +/- 40 mOsm. Some claims are further drawn to the medium Brookfield viscosity at 20 °C in the range between 1-15 centipoises or 2.5-10 centipoises. Some claims are further drawn to the exclusion of dextran.

The cited documents WO 96/32929 (IDS reference) and US 5,102,783 (Alkemade et al) are relied upon as explained above for the disclosure of a preservation media for living organs, biological tissues and cells wherein the media comprise a high-molecular-weight HA and a

sodium chloride in amounts as required by the claimed invention as well as trace elements, amino acids, vitamins and stabilizing pH buffer.

The DERWENT publication XP 002036193 of JP 6107538 also discloses a preservation medium for living organs, tissues and cells of eye ball cornea transplant wherein the medium comprises a liquid nutritive base, a high-molecular-weight hyaluronic acid and sodium chloride in amounts as required by the claimed invention. The cited medium as disclosed contains 0.05-05 % (500-5000 mg/L) of hyaluronic acid (HA), abut 5 g/L or 0.5 % of sodium chloride.

All cited documents WO 96/32929 (IDS reference), US 5,102,783 (Alkemade et al) and DERWENT publication clearly teach that the media are free from components of animal origin and the cited media do not contain dextran. Moreover, the cited US 5,102,783 explicitly teaches substitution of HA for serum or for a component of animal origin for the benefit in reducing potential microbial and viral contaminations. The cited DERWENT publication XP 002036193 of JP 6107538 explicitly discloses that the exclusion of dextran provides for similar or superior effects as the HA-containing composition.

The medium of the cited DERWENT publication XP 002036193 of JP 6107538 is lacking additional components such as poloxamer 188 and methyl cellulose. But the other cited documents WO 96/32929 and US 5,102,783 (Alkemade et al) teach incorporation of additional viscosity agents and/or surfactants in the HA-containing medium for preservation and minimizing traumatic effects on living organs, biological tissues and cells. In particular, WO 96/32929 teach incorporation of additional viscosity agent such as methyl cellulose in the HA-containing medium. US 5,102,783 (Alkemade et al) teaches incorporation of additional viscosity agents or surfactants such as poloxamer 188 in the HA-containing medium.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to add poloxamer 188 and/or methyl cellulose to the HA-containing medium of the cited DERWENT publication XP 002036193 of JP 6107538 with a reasonable expectation of success in preserving and minimizing traumatic effects on living organs, biological tissues and cells because the prior art teaches and suggests incorporation of additional viscosity agents and/or surfactants including poloxamer 188 and/or methyl cellulose in the HA-containing medium for preserving and minimizing traumatic effects on living organs, biological tissues and cells as adequately taught by WO 96/32929 and US 5,102,783 (Alkemade et al). Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Claims 1-8, 10 and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over DERWENT publication XP 002036193 of JP 6107538 (IDS reference), WO 96/32929 (IDS reference) and US 5,102,783 (Alkemade et al) as applied to claims 1-8, 10 and 16-21 above, and further in view of US 6,153,582 (Skelnik).

Claims 1-8, 10 and 16-21 as above. Claim 15 is further drawn to incorporation of chondroitin sulfate, heparin sulfate, alginic acid and starch into the preservation medium.

The cited WO 96/32929 and US 5,102,783 (Alkemade et al) and the DERWENT publication are relied upon as explained above for the disclosure of preservation media for living organs, biological tissues and cells wherein the medium comprises a high-molecular-weight

hyaluronic acid, sodium chloride, trace elements, amino acids, vitamins and stabilizing pH buffer; and wherein the medium is free from components of animal origin. The cited media are lacking chondroitin sulfate, heparin sulfate, alginic acid and starch in the preservation medium. But US 6,153,582 (Skelnik) teaches incorporation of chondroitin sulfate, heparin sulfate, alginic acid and starch into the preservation medium (enter document including col. 3, lines 55-65).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to add chondroitin sulfate, heparin sulfate, alginic acid and starch into the preservation media with a reasonable expectation of success in preserving and minimizing traumatic effects on living organs, biological tissues and cells because these components have been known and used in the prior art compositions designed for preserving and minimizing traumatic effects on living organs, biological tissues and cells. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary. The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 1/04/2010 have been fully considered but they are not all persuasive.

Claim rejection under 35 U.S.C. 102(b) as being anticipated by DERWENT publication XP 002036193 of JP 6107538 (IDS reference) has been withdrawn because the cited DERWENT publication does not discloses incorporation of aminoacids and/or vitamins in the

preservation medium. Applicants' argument that the disclosed medium contain HA of microbial origin and thus, animal component is not well taken because microorganisms are not animals.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by WO 96/32929 applicants argue that the cited preservation medium does not contain aminoacids and/or vitamins as required by claim 1. Yet, the present claim 1 and the applicants' disclosure (pages 9-13) are generic with regard to aminoacids and/or vitamins. Thus, glutathione that is clearly incorporated into the medium of WO 96/32929 (see page 7, for example) would provide for generic aminoacids (cysteine and glutamine are components of glutathione) and generic vitamins (organic compounds optionally with amines) with within the meaning of the claims and when read in the light of specification.

With regard to claim rejection under 35 U.S.C. 102(b) as being anticipated by US 5,102,783 (Alkemade et al) applicants appear to argue than the cited medium is intended for *in vivo* applications that have different requirements than *in vitro* applications. However, the instant claims are directed to a product but not to a method. Moreover, US 5,102,783 (Alkemade et al) clearly states that its medium composition with HA is intended for culturing and freezing cells and, thus for *in vitro* applications.

With regard to claim rejection under 35 USC § 103 applicants argue that there is no suggestion to combine references. However, the cited references are in the same field of endeavor (such as compositions intended for cell preservation) and they seek to solve the same problems as the instant application and claims (such as provide for cell preservation compositions), and one of skill in the art is free to select components available in the prior art, *In re* Winslow, 151 USPQ 48 (CCPA, 1966).

Applicants also appear to argue some unexpected results or effects provided by the medium of the instant invention as intended for extended periods of preservation at a wide range of temperatures (response page 8, last par.). However, the scope of the showing must be commensurate with the scope of claims to consider evidence probative of unexpected results, for example. In re Dill, 202 USPQ 805 (CCPA, 1979), In re Lindner 173 USPQ 356 (CCPA 1972), In re Hyson, 172 USPQ 399 (CCPA 1972), In re Boesch, 205 USPQ 215, (CCPA 1980), In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983), In re Clemens, 206 USPQ 289 (CCPA 1980). It should be clear that the probative value of the data is not commensurate in scope with the degree of protection sought by the claim. The instant claim 1 is generic with regard to specific components and their specific amounts in order to consider the evidence necessary to overcome a prima facie case of obviousness.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

March 26, 2010

/Vera Afremova/

Primary Examiner, Art Unit 1657